Generation of tissue-engineered small intestine using embryonic stem cell-derived human intestinal organoids.

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Authors: Stacy R Finkbeiner, Jennifer J Freeman, Minna M Wieck, Wael El-Nachef, Christopher H Altheim, Yu-Hwai Tsai, Sha Huang, Rachel Dyal, Eric S White, Tracy C Grikscheit, Daniel H Teitelbaum, Jason R Spence

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Public Summary:
Short bowel syndrome (SBS) is characterized by poor nutrient absorption due to a deficit of healthy intestine. Current treatment practices rely on providing supportive medical therapy with parenteral nutrition; while life saving, such interventions are not curative and are still associated with significant co-morbidities. As approaches to lengthen remaining intestinal tissue have been met with only limited success and intestinal transplants have poor survival outcomes, new approaches to treating SBS are necessary. Human intestine derived from embryonic stem cells (hESCs) or induced pluripotent stem cells (iPSCs), called human intestinal organoids (HIOs), have the potential to offer a personalized and scalable source of intestine for regenerative therapies. However, given that HIOs are small three-dimensional structures grown in vitro, methods to generate usable HIO-derived constructs are needed. We investigated the ability of hESCs or HIOs to populate acellular porcine intestinal matrices and artificial polyglycolic/poly L lactic acid (PGA/PLLA) scaffolds, and examined the ability of matrix/scaffolds to thrive when transplanted in vivo. Our results demonstrate that the acellular matrix alone is not sufficient to instruct hESC differentiation towards an endodermal or intestinal fate. We observed that while HIOs reseed acellular porcine matrices in vitro, the HIO-reseeded matrices do not thrive when transplanted in vivo. In contrast, HIO-seeded PGA/PLLA scaffolds thrive in vivo and develop into tissue that looks nearly identical to adult human intestinal tissue. Our results suggest that HIO-seeded PGA/PLLA scaffolds are a promising avenue for developing the mucosal component of tissue engineered human small intestine, which need to be explored further to develop them into fully functional tissue.

Scientific Abstract:
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